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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/719,067 | 08/16/2001 | David B. Weiner | UPN-3695 | 4038 |

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| EXAMINER | |
|---|---|
| SHUKLA, RAM R | |
| **ART UNIT** | **PAPER NUMBER** |
| 1632 | |

DATE MAILED: 03/24/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/719,067 | WEINER ET AL. | |
| | Examiner | Art Unit | |
| | Ram R. Shukla | 1632 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1,2 and 5-31* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2 and 5-31* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

## DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 01-08-2004 has been entered.

2. Claims 1, 2, 5-31 are pending. Applicant's elected CD156 promoter in Paper No. 9.

3. The 1.132 declaration by Dr. David B. Weiner has been entered and considered.

### *Claim Rejections - 35 USC § 112*

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 1-2 and 6-8, 18-24, 29 and 30 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claimed invention as instantly recited encompasses a method comprising administering a DNA molecule comprising any macrophage specific promoter from source.

When the claims are analyzed in light of the specification, instant invention encompasses any macrophage specific promoter from source. However, the specification discloses only catalase, CD156, M-CSFR, p73, and FcgRI. In analyzing whether the written description requirement is met for genus claims, it is first determined whether a representative number of species have been described by their complete structure. In the instant case, the specification list promoters for genes taught in the art. As indicated above catalase, CD156, M-CSFR, p73, and FcgRI are the only species whose complete structure was disclosed in the art. The specification does not provide any disclosure as to what would have been the structure of a representative number of macrophage specific promoters of the genus claimed. Next, then, it is determined whether a representative number of species have been sufficiently described by other relevant identifying characteristics (i.e. other than nucleotide sequence), specific features and functional attributes that would distinguish different members of the claimed genus. In the instant case, the only identifying characteristic is that they are macrophage specific or specific for cells of macrophage derived lineage. The specification does not describe what is the origin of these promoters or how are the promoter for these conserved across the species and what are their identifying characteristics. In regard to polynucleotides from any animal species, it is noted that the specification does not provide any disclosure whether these sequences from other species would have had same characteristics, would have had additional characteristics or properties.

Applicants' attention is directed to the decision in *In re Shokal*, 113 USPQ 283 (CCPA 1957) wherein is stated:

> It appears to be well settled that a single species can rarely, if ever, afford sufficient support for a generic claim. In re Soll, 25 C.C.P.A. (Patents) 1309, 97 F.2d 623, 38 USPQ 189; In re Wahlforss et al., 28 C.C.P.A. (Patents) 867, 117 F.2d 270, 48 USPQ 397. The decisions do not however fix any definite number of species which will establish completion of a generic invention and it seems evident therefrom that such number will vary, depending on the circumstances of particular cases. Thus, in the case of small genus such as the halogens, consisting of four species, a reduction to practice of three, or perhaps even two, might serve to complete the generic invention, while in the case of a genus comprising hundreds of species, a considerably larger number of reductions to practice would probably be necessary.

In conclusion, this limited information is not deemed sufficient to reasonably convey to one skilled in the art that Applicant is in possession of macrophage specific promoters for the broad genus claimed. Thus it is concluded that the written description requirement is not satisfied for the claimed genus.

6. Claims 1-2 and 5-8 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an method of delivering a protein to a macrophage cell or a cell of macrophage derived lineage in vitro or in vivo, comprising intramuscular administration of a plasmid DNA molecule wherein a nucleotide sequence encoding the protein is operably linked to a macrophage specific promoter and a polyA signal that is functional in macrophage cell or a cell of macrophage derived lineage, wherein said macrophage specific promoter is selected from the list a catalase promoter, a CD156 promoter, a M-CSFR promoter, a p73 promoter and an FcyRI promoter, wherein said plasmid DNA molecule is taken up by a macrophage cell or a cell of macrophage derived lineage and wherein said nucleotide sequence is expressed to produce said protein in said macrophage cell or said cell of macrophage derived lineage, not reasonably provide enablement for other embodiments for reasons of record set forth in the previous office action of 3-27-03 and 8-8-03 and as discussed below. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claims 9-31 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention for reasons of record set forth in the previous office action of 3-27-03 and 8-8-03.

***Response to Arguments***

Applicant's arguments filed 1-8-04 have been fully considered but they are not persuasive to obviate all the rejections. It is noted that the enablement rejection of claims 1-2 and 5-8 has been modified in view of applicants' arguments and the declaration by Dr. Weiner. However, neither the declaration nor the applicants' arguments are sufficient to obviate all the grounds of rejections and issues raised.

Applicants have argued:

"The crux of the rejection as discussed in the Final Office Action, the Advisory Action, and the telephonic interview (October 27, 2003) is that there is no evidence in the specification or in the art of the record that it would not be routine to be able to identify a lymph node and be able to deliver to a lymph node a DNA molecule."

However, these arguments are not persuasive and do not represent the real enablement issues presented in the previous office actions. The issue are: the unpredictability of the art of targeted delivery of a protein to a tissue, including a lymph node by administering any vector comprising any promoter by any route. It is emphasized that the all the claims are not limited to macrophage specific promoter. While identifying a lymph node and delivering a dye to the lymph node by injecting may be routine, in the instant invention, the issue is: delivery of any one or more DNA molecule(s) comprising any promoter driving the expression of a protein to any site that is proximal to a lymph node such that the DNA is taken up by macrophage cells at the site, expressed in the cell and the protein is then delivered to the lymph node resulting in cell elimination in the lymph node or immune respone production. Neither the specification nor the art of record nor the declaration address the issue or provide enabling teachings and guidance. There is no evidence that two DNA molecules injected at a site would enter the same cell, would express the protein in sufficient amounts such that the protein drained to the lymph node in sufficient quantity to kill the cells or produce immune response.

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 9-17 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 9-17 are indefinite because it is unclear as to what is meant by the term "a site on said individual's body that is proximal to said lymph node". The metes and bounds of the claimed invention are not clear because the word "proximal" is relative and an artisan would not know what is encompassed by the claimed invention.

Claim 12 is idefinite because it recites "said promoter is a macrophage promoter". It is unclear as to what is a macrophage promoter.

9. The 102 and 103 rejection of claims 1-2 and 5-8 is withdrawn in view of applicants' arguments.

10. Claims 1-2 and 5-8 would be allowable if written in conformation with the scope of enablement rejection set forth above.

11. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ram R. Shukla whose telephone number is (571) 272-0735 . The examiner can normally be reached on Monday through Friday from 7:30 am to 4:00 p.m. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson, can be reached at (571) 272-0804. The fax phone number for TC 1600 is (703) 703-872-9306. Any inquiry of a general nature, formal matters or relating to the status of this application or

proceeding should be directed to the William Phillips whose telephone number is (571) 272-0548.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Ram R. Shukla, Ph.D.
Primary Examiner
Art Unit 1632

RAM R. SHUKLA, PH.D.
PRIMARY EXAMINER